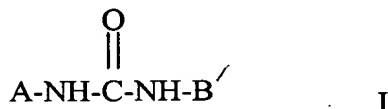


5

WHAT IS CLAIMED IS:

10 1. A method for the treatment of a disease mediated by p38 other than cancer, comprising administering a compound of formula I



wherein B is a substituted or unsubstituted, up to tricyclic, aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 5- or 6-member aromatic structure containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur, wherein if B is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of halogen, up to per-halosubstitution, and X_n ,

wherein n is 0-3 and each X is independently selected from the group consisting of $-\text{CN}$, $-\text{CO}_2\text{R}^5$, $-\text{C}(\text{O})\text{NR}^5\text{R}^{5'}$, $-\text{C}(\text{O})\text{R}^5$, $-\text{NO}_2$, $-\text{OR}^5$, $-\text{SR}^5$, $-\text{NR}^5\text{R}^{5'}$, $-\text{NR}^5\text{C}(\text{O})\text{OR}^{5'}$, $-\text{NR}^5\text{C}(\text{O})\text{R}^{5'}$, $\text{C}_1\text{-C}_{10}$ alkyl, $\text{C}_2\text{-C}_{10}$ alkenyl, $\text{C}_1\text{-C}_{10}$ alkoxy, $\text{C}_3\text{-C}_{10}$ cycloalkyl, $\text{C}_6\text{-C}_{14}$ aryl, $\text{C}_7\text{-C}_{24}$ alkaryl, $\text{C}_3\text{-C}_{13}$ heteroaryl, $\text{C}_4\text{-C}_{23}$ alkheteroaryl, substituted $\text{C}_1\text{-C}_{10}$ alkyl, substituted $\text{C}_2\text{-C}_{10}$ alkenyl, substituted $\text{C}_1\text{-C}_{10}$ alkoxy, substituted $\text{C}_3\text{-C}_{10}$ cycloalkyl, substituted $\text{C}_4\text{-C}_{23}$ alkheteroaryl and $-\text{Y-Ar}$;

wherein if X is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of $-\text{CN}$, $-\text{CO}_2\text{R}^5$, $-\text{C}(\text{O})\text{R}^5$, $-\text{C}(\text{O})\text{NR}^5\text{R}^{5'}$, $-\text{OR}^5$, $-\text{SR}^5$, $-\text{NR}^5\text{R}^{5'}$, $-\text{NO}_2$, $-\text{NR}^5\text{C}(\text{O})\text{R}^{5'}$, $-\text{NR}^5\text{C}(\text{O})\text{OR}^{5'}$ and halogen up to per-halosubstitution;

wherein R^5 and $\text{R}^{5'}$ are independently selected from H, $\text{C}_1\text{-C}_{10}$ alkyl, $\text{C}_2\text{-C}_{10}$ alkenyl, $\text{C}_3\text{-C}_{10}$ cycloalkyl, $\text{C}_6\text{-C}_{14}$ aryl, $\text{C}_3\text{-C}_{13}$ heteroaryl, $\text{C}_7\text{-C}_{24}$ alkaryl, $\text{C}_4\text{-C}_{23}$ alkheteroaryl, up to per-halosubstituted $\text{C}_1\text{-C}_{10}$ alkyl, up to per-halosubstituted $\text{C}_3\text{-C}_{10}$

cycloalkyl, up to per-halosubstituted C₂-C₁₀ alkenyl, up to per-halosubstituted C₆-C₁₄ aryl and up to per-halosubstituted C₃-C₁₃ heteroaryl,

wherein Y is -O-, -S-, -N(R⁵)-, -(CH₂)_m-, -C(O)-, -CH(OH)-, -(CH₂)_mO-,
 -(CH₂)_mS-, -(CH₂)_mN(R⁵)-, -O(CH₂)_m-, -CHX^a-, -NR⁵C(O)NR⁵R^{5'}-, -NR⁵C(O)-,
 -C(O)NR⁵-, -CX^a₂-, -S-(CH₂)_m- and -N(R⁵)(CH₂)_m-,

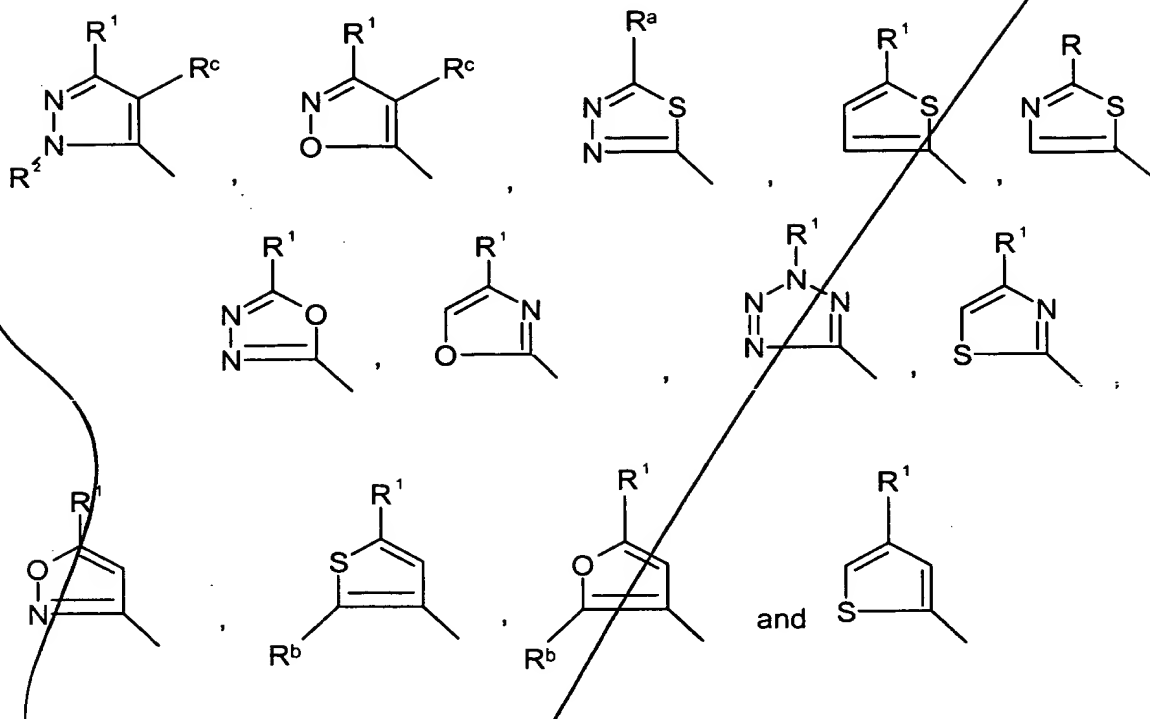
m = 1-3, and X^a is halogen; and

Ar is a 5-10 member aromatic structure containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur which is unsubstituted or substituted by halogen up to per-halosubstitution and optionally substituted by Z_{n1},

wherein n1 is 0 to 3 and each Z is independently selected from the group consisting of -CN, -CO₂R⁵, -C(O)NR⁵R^{5'}, -C(O)-NR⁵, -NO₂, =O, -OR⁵, -SR⁵, -NR⁵R^{5'}, -C(O)R⁵, -SO₂R⁵, -SO₂NR⁵R^{5'}, -NR⁵C(O)OR^{5'}, -NR⁵C(O)R^{5'}, C₁-C₁₀ alkyl, C₁-C₁₀ alkoxy, C₃-C₁₀ cycloalkyl, C₆-C₁₄ aryl, C₃-C₁₃ heteroaryl, C₇-C₂₄ alkaryl, C₄-C₂₃ alkheteroaryl, substituted C₁-C₁₀ alkyl, substituted C₃-C₁₀ cycloalkyl, substituted C₇-C₂₄ alkaryl and substituted C₄-C₂₃ alkheteroaryl;

wherein if Z is a substituted group, it is substituted by the one or more substituents independently selected from the group consisting of -CN, -CO₂R⁵, -C(O)R⁵, -C(O)NR⁵R^{5'}, =O, -OR⁵, -SR⁵, -NO₂, -NR⁵R^{5'}, -NR⁵C(O)R^{5'}, -NR⁵C(O)OR^{5'}, C₁-C₁₀ alkyl, C₁-C₁₀ alkoxy, C₃-C₁₀ cycloalkyl, C-C₁₀ heteroaryl, C₆-C₁₄ aryl, C₄-C₂₄ alkheteroaryl and C₇-C₂₄ alkaryl;

A is a heteroaryl moiety selected from the group consisting of



5 wherein

R^1 is selected from the group consisting of halogen, C_3 - C_{10} alkyl, C_3 - C_{10} cycloalkyl, C_1 - C_{13} heteroaryl, C_6 - C_{14} aryl, C_7 - C_{24} alkaryl, up to per-halosubstituted C_1 - C_{10} alkyl, up to per-halosubstituted C_3 - C_{10} cycloalkyl, up to per-halosubstituted C_1 - C_{13} heteroaryl, up to per-halosubstituted C_6 - C_{14} aryl, and up to per-halosubstituted C_7 - C_{24} alkaryl;

R^2 is selected from the group consisting of H, $-C(O)R^4$, $-CO_2R^4$, $-C(O)NR^3R^{3'}$, C_1 - C_{10} alkyl, C_3 - C_{10} cycloalkyl, C_7 - C_{24} alkaryl, C_4 - C_{23} alkheteroaryl, substituted C_1 - C_{10} alkyl, substituted C_3 - C_{10} cycloalkyl, substituted C_7 - C_{24} alkaryl and substituted C_4 - C_{23} alkheteroaryl,

15 where R^2 is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of $-CN$, $-CO_2R^4$, $-C(O)NR^3R^{3'}$, $-NO_2$, $-OR^4$, $-SR^4$, and halogen up to per-halosubstitution,

wherein R^3 and $R^{3'}$ are independently selected from the group consisting of H, $-OR^4$, $-SR^4$, $-NR^4R^{4'}$, $-C(O)R^4$, $-CO_2R^4$, $-C(O)NR^4R^{4'}$, C_1 - C_{10} alkyl, C_3 - C_{10} cycloalkyl,

C₆-C₁₄ aryl, C₃-C₁₃ heteroaryl, C₇-C₂₄ alkaryl, C₄-C₂₃ alkheteroaryl, up to per-halosubstituted C₁-C₁₀ alkyl, up to per-halosubstituted C₃-C₁₀ cycloalkyl, up to per-halosubstituted C₆-C₁₄ aryl and up to per-halosubstituted C₃-C₁₃ heteroaryl; and

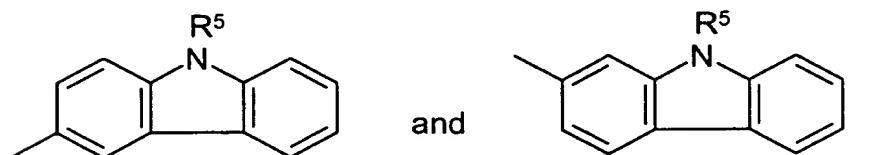
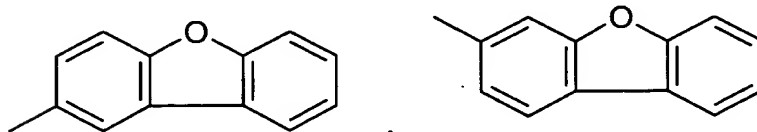
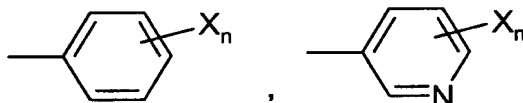
wherein R⁴ and R^{4'} are independently selected from the group consisting of H, C₁-C₁₀ alkyl, C₃-C₁₀ cycloalkyl, C₆-C₁₄ aryl, C₃-C₁₃ heteroaryl; C₇-C₂₄ alkaryl, C₄-C₂₃ alkheteroaryl, up to per-halosubstituted C₁-C₁₀ alkyl, up to per-halosubstituted C₃-C₁₀ cycloalkyl, up to per-halosubstituted C₆-C₁₄ aryl and up to per-halosubstituted C₃-C₁₃ heteroaryl,

R^a is C₁-C₁₀ alkyl, C₃-C₁₀ cycloalkyl, up to per-halosubstituted C₁-C₁₀ alkyl and up to per-halosubstituted C₃-C₁₀ cycloalkyl; and

R^b is hydrogen or halogen,

R^c is hydrogen, halogen, C₁-C₁₀ alkyl, up to per-halosubstituted C₁-C₁₀ alkyl or combines with R¹ and the ring carbon atoms to which R¹ and R^c are bound to form a 5- or 6-membered cycloalkyl, aryl or heteroaryl ring with 0-2 members selected from O, N and S.

2. A method as in claim 1, wherein B is up to a tricyclic aromatic ring structure selected from the group consisting of



which is substituted or unsubstituted by halogen, up to per-halosubstitution, and

wherein $n = 0-3$ and each X is independently selected from the group consisting of $-\text{CN}$, $-\text{CO}_2\text{R}^5$, $-\text{C}(\text{O})\text{NR}^5\text{R}^{5'}$, $-\text{C}(\text{O})\text{R}^5$, $-\text{NO}_2$, $-\text{OR}^5$, $-\text{SR}^5$, $-\text{NR}^5\text{R}^{5'}$, $-\text{NR}^5\text{C}(\text{O})\text{OR}^{5'}$, $-\text{NR}^5\text{C}(\text{O})\text{R}^{5'}$, $\text{C}_1\text{-C}_{10}$ alkyl, C_{2-10} -alkenyl, C_{1-10} -alkoxy, $\text{C}_3\text{-C}_{10}$ cycloalkyl, $\text{C}_6\text{-C}_{14}$ aryl, $\text{C}_7\text{-C}_{24}$ alkaryl, $\text{C}_3\text{-C}_{13}$ heteroaryl, $\text{C}_4\text{-C}_{23}$ alkheteroaryl, and substituted $\text{C}_1\text{-C}_{10}$ alkyl, substituted C_{2-10} -alkenyl, substituted C_{1-10} -alkoxy, substituted $\text{C}_3\text{-C}_{10}$ cycloalkyl, substituted $\text{C}_4\text{-C}_{23}$ alkheteroaryl and $-\text{Y-Ar}$;

wherein if X is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of $-\text{CN}$, $-\text{CO}_2\text{R}^5$, $-\text{C}(\text{O})\text{R}^5$, $-\text{C}(\text{O})\text{NR}^5\text{R}^{5'}$, $-\text{OR}^5$, $-\text{SR}^5$, $-\text{NR}^5\text{R}^{5'}$, NO_2 , $-\text{NR}^5\text{C}(\text{O})\text{R}^{5'}$, $-\text{NR}^5\text{C}(\text{O})\text{OR}^{5'}$ and halogen up to per-halosubstitution;

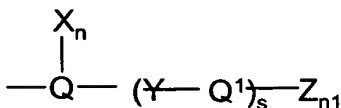
wherein R^5 and $\text{R}^{5'}$ are independently selected from H , $\text{C}_1\text{-C}_{10}$ alkyl, C_{2-10} -alkenyl, $\text{C}_3\text{-C}_{10}$ cycloalkyl, $\text{C}_6\text{-C}_{14}$ aryl, $\text{C}_3\text{-C}_{13}$ heteroaryl, $\text{C}_7\text{-C}_{24}$ alkaryl, $\text{C}_4\text{-C}_{23}$ alkheteroaryl, up to per-halosubstituted $\text{C}_1\text{-C}_{10}$ alkyl, up to per-halosubstituted C_{2-10} -alkenyl, up to per-halosubstituted $\text{C}_3\text{-C}_{10}$ cycloalkyl, up to per-halosubstituted $\text{C}_6\text{-C}_{14}$ aryl and up to per-halosubstituted $\text{C}_3\text{-C}_{13}$ heteroaryl,

wherein Y is $-\text{O}-$, $-\text{S}-$, $-\text{N}(\text{R}^5)-$, $-(\text{CH}_2)_m-$, $-\text{C}(\text{O})-$, $-\text{CH}(\text{OH})-$, $-(\text{CH}_2)_m\text{O}-$, $-\text{NR}^5\text{C}(\text{O})\text{NR}^5\text{R}^{5'}$, $-\text{NR}^5\text{C}(\text{O})-$, $-\text{C}(\text{O})\text{NR}^5-$, $-(\text{CH}_2)_m\text{S}-$, $-(\text{CH}_2)_m\text{N}(\text{R}^5)-$, $-\text{O}(\text{CH}_2)_m-$, $-\text{CHX}^a$, $-\text{CX}^a_2-$, $-\text{S}-(\text{CH}_2)_m-$ and $-\text{N}(\text{R}^5)(\text{CH}_2)_m-$,

$m = 1-3$, and X^a is halogen; and

Ar is a 5-10 member aromatic structure containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur which is unsubstituted or substituted by halogen up to per-halo and optionally substituted by Z_{n1} , wherein $n1$ is 0 to 3 and each Z is independently selected from the group consisting of $-\text{CN}$, $-\text{CO}_2\text{R}^5$, $-\text{C}(\text{O})\text{R}^5$, $=\text{O}$, $-\text{SO}_2\text{R}^5$, $-\text{SO}_2\text{NR}^5\text{R}^{5'}$, $-\text{C}(\text{O})\text{NR}^5\text{R}^{5'}$, $-\text{C}(\text{O})\text{R}^5$, $-\text{NO}_2$, $-\text{OR}^5$, $-\text{SR}^5$, $-\text{NR}^5\text{R}^{5'}$, $-\text{NR}^5\text{C}(\text{O})\text{OR}^{5'}$, $-\text{NR}^5\text{C}(\text{O})\text{R}^{5'}$, $\text{C}_1\text{-C}_{10}$ alkyl, $\text{C}_1\text{-C}_{10}$ alkoxy, $\text{C}_3\text{-C}_{10}$ cycloalkyl, $\text{C}_6\text{-C}_{14}$ aryl, $\text{C}_3\text{-C}_{13}$ heteroaryl, $\text{C}_7\text{-C}_{24}$ alkaryl, $\text{C}_4\text{-C}_{23}$ alkheteroaryl, substituted $\text{C}_1\text{-C}_{10}$ alkyl, substituted $\text{C}_3\text{-C}_{10}$ cycloalkyl, substituted $\text{C}_7\text{-C}_{24}$ alkaryl and substituted $\text{C}_4\text{-C}_{23}$ alkheteroaryl; wherein if Z is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of $-\text{CN}$, $-\text{CO}_2\text{R}^5$, $-\text{C}(\text{O})\text{NR}^5\text{R}^{5'}$, $=\text{O}$, $-\text{OR}^5$, $-\text{SR}^5$, $-\text{NO}_2$, $-\text{NR}^5\text{R}^{5'}$, $-\text{NR}^5\text{C}(\text{O})\text{R}^{5'}$, $-\text{NR}^5\text{C}(\text{O})\text{OR}^{5'}$, $\text{C}_1\text{-C}_{10}$ alkyl, $\text{C}_1\text{-C}_{10}$ alkoxy, $\text{C}_3\text{-C}_{10}$ cycloalkyl, C-C_{10} heteroaryl, $\text{C}_6\text{-C}_{14}$ aryl, $\text{C}_4\text{-C}_{24}$ alkheteroaryl and $\text{C}_7\text{-C}_{24}$ alkaryl.

3. A method of claim 1, wherein B is



wherein Y is selected from the group consisting of -O-, -S-, -CH₂-, -SCH₂-, -CH₂S-, -CH(OH)-, -C(O)-, -CX^a₂, -CX^aH-, -CH₂O- and -OCH₂-, where X^a is halogen,

- 5 Q is a six member aromatic structure containing 0-2 nitrogen, substituted or unsubstituted by halogen, up to per-halosubstitution;

Q¹ is a mono- or bicyclic aromatic structure of 3 to 10 carbon atoms and 0-4 members of the group consisting of N, O and S, unsubstituted or unsubstituted by halogen up to per-halosubstitution, and

- 10 X, Z, n and n1 are as defined in claim 1 and s is 0 or 1.

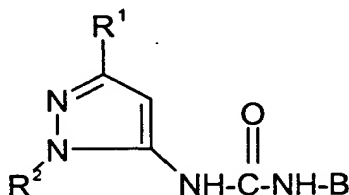
4. A method as in claim 3, wherein

Q is phenyl or pyridinyl, substituted or unsubstituted by halogen, up to per-halosubstitution,

- 15 Q¹ is selected from the group consisting of phenyl, pyridinyl, naphthyl, pyrimidinyl, quinoline, isoquinoline, imidazole and benzothiazolyl, substituted or unsubstituted by halogen, up to per-halo substitution, or -Y-Q¹ is phthalimidinyl substituted or unsubstituted by halogen up to per-halo substitution, and

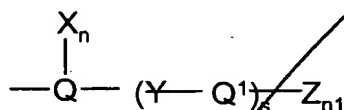
- 20 Z and X are independently selected from the group consisting of -R⁶, -OR⁶ and -NHR⁷, wherein R⁶ is hydrogen, C₁-C₁₀-alkyl or C₃-C₁₀-cycloalkyl and R⁷ is selected from the group consisting of hydrogen, C₃-C₁₀-alkyl, C₃-C₆-cycloalkyl and C₆-C₁₀-aryl, wherein R⁶ and R⁷ can be substituted by halogen or up to per-halosubstitution.

- 25 5. A method as in claim 1, comprising administering a compound of the formula



wherein R¹ and R² and B are as defined in claim 1.

6. A method as in claim 5, wherein B is 2,3-dichlorophenyl or of the formula



wherein Q is phenyl, Q¹ is phenyl or pyridinyl, Y is -O-, -S-, -CH₂- or -SCH₂, X is CF₃, and Z is -OH, -Cl or NHC(O)-C_pH_{2p+1}, where p = 2-4, s = 0 or 1, n = 0 and n1 = 0 or 1.

7. A method as in claim 1 comprising administering a compound selected from the group consisting of:

N-(3-*tert*-Butyl-5-pyrazolyl)-*N'*-(4-(2,3-dichlorophenyl)urea;

N-(3-*tert*-Butyl-5-pyrazolyl)-*N'*-(3-(4-pyridinyl)thiophenyl)urea;

N-(3-*tert*-Butyl-5-pyrazolyl)-*N'*-(4-(4-pyridinyl)methylphenyl)urea;

N-(3-*tert*-Butyl-5-pyrazolyl)-*N'*-(4-(4-pyridinyl)oxyphenyl)urea;

N-(3-*tert*-Butyl-5-pyrazolyl)-*N'*-(4-(4-pyridinyl)thiophenyl)urea;

N-(3-*tert*-Butyl-5-pyrazolyl)-*N'*-(4-(4-pyridinyl)methylphenyl)urea;

N-(1-Methyl-3-*tert*-butyl-5-pyrazolyl)-*N'*-(2,3-dichlorophenyl)urea;

N-(1-Methyl-3-*tert*-butyl-5-pyrazolyl)-*N'*-(4-(4-hydroxy-

phenyl)thiophenyl)urea;

N-(1-Methyl-3-*tert*-butyl-5-pyrazolyl)-*N'*-(4-(4-ethylaminocarbonyl-

phenyl)oxyphenyl)urea;

N-(1-Methyl-3-*tert*-butyl-5-pyrazolyl)-*N'*-(4-(4-isobutylaminocarbonyl-

phenyl)thiophenyl)urea;

N-(1-Methyl-3-*tert*-butyl-5-pyrazolyl)-*N'*-(4-(4-pyridinyl)thiophenyl)urea;

N-(1-Methyl-3-*tert*-butyl-5-pyrazolyl)-*N'*-(3-(4-pyridinyl)thiophenyl)urea;

N-(1-Methyl-3-*tert*-butyl-5-pyrazolyl)-*N'*-(4-(4-pyridinyl)thio-3-(trifluoromethyl)phenyl)urea;

N-(1-Methyl-3-*tert*-butyl-5-pyrazolyl)-*N'*-(4-(4-pyridinyl)oxyphenyl)urea;

N-(1-Methyl-3-*tert*-butyl-5-pyrazolyl)-*N'*-(4-((4-pyridinyl)methylthio)-phenyl)urea;

N-(1-(2,2,2-Trifluoroethyl)-3-*tert*-butyl-5-pyrazolyl)-*N'*-(2,3-dichloro-phenyl)urea;

N-(1-(2-Hydroxyethyl)-3-*tert*-butyl-5-pyrazolyl)-*N'*-(2,3-dichlorophenyl)urea;

N-(1-Ethoxycarbonylmethyl-3-*tert*-butyl-5-pyrazolyl)-*N'*-(2,3-dichloro-phenyl)urea;

N-(1-(2-Cyanoethyl)-3-*tert*-butyl-5-pyrazolyl)-*N'*-(2,3-dichlorophenyl)urea;

N-(1-(3-Hydroxyphenyl)methyl-3-*tert*-butyl-5-pyrazolyl)-*N'*-(2,3-dichloro-phenyl)urea;

N-(1-Cyclohexyl-3-*tert*-butyl-5-pyrazolyl)-*N'*-(4-(4-pyridinyl)methyl-phenyl)urea;

N-(1-methyl-3-phenyl-5-pyrazolyl)-*N'*-(3-(4-(2-methylcarbamoyl)-pyridyl)thiophenyl) urea;

N-(1-methyl-3-*tert*-butyl-5-pyrazolyl)-*N'*-(4-(4-pyridyl)thiophenyl) urea;

N-(1-methyl-3-*tert*-butyl-5-pyrazolyl)-*N'*-(3-(4-pyridyl)thiophenyl) urea;

N-(1-methyl-3-*tert*-butyl-5-pyrazolyl)-*N'*-(3-trifluoromethyl-4-(4-pyridylthio)phenyl) urea;

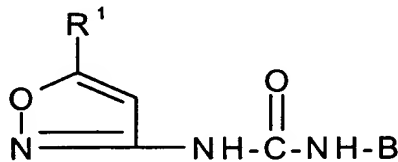
N-(3-*tert*-butyl-5-pyrazolyl)-*N'*-(3-(4-pyridyl)oxyphenyl) urea;

N-(3-*tert*-butyl-5-pyrazolyl)-*N'*-(4-(4-pyridyl)oxyphenyl) urea;

and pharmaceutically acceptable salts thereof.

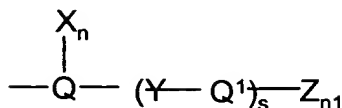
8. A method as in claim 5, wherein R¹ is t-butyl.

9. A method as in claim 1 comprising administering a compound of the formula



wherein R¹ and B are as defined in claim 1.

10. A method as in claim 9, wherein B is



wherein Q is phenyl, Q¹ is phenyl or pyridinyl, Y is -O-, -S- or -CH₂, X is CF₃, Z is OH, CH₃, -O-C_pH_{2p+1}, wherein n = 2-6 or -C(O)-NH-CH₃, s = 1, n = 0 or 1 and n1 = 0 or 1.

5

11. A method as in claim 1 comprising administering a compound selected from the group consisting of:

N-(5-*tert*-Butyl-3-isoxazolyl)-*N*'-(4-(4-hydroxyphenyl)oxyphenyl)urea;

N-(5-*tert*-Butyl-3-isoxazolyl)-*N*'-(4-(4-isopropoxyphenyl)oxyphenyl)urea;

N-(5-*tert*-Butyl-3-isoxazolyl)-*N*'-(4-(4-isobutoxyphenyl)oxyphenyl)urea;

N-(5-*tert*-Butyl-3-isoxazolyl)-*N*'-(4-(4-pentyloxyphenyl)oxyphenyl)urea;

N-(5-*tert*-Butyl-3-isoxazolyl)-*N*'-(4-(4-methylaminocarbonylphenyl)-

oxyphenyl)urea;

N-(5-*tert*-Butyl-3-isoxazolyl)-*N*'-(3-(4-pyridinyl)thiophenyl)urea;

N-(5-*tert*-Butyl-3-isoxazolyl)-*N*'-(3-(4-pyridinyl)oxyphenyl)urea;

N-(5-*tert*-Butyl-3-isoxazolyl)-*N*'-(4-(4-pyridinyl)oxyphenyl)urea;

N-(5-*tert*-Butyl-3-isoxazolyl)-*N*'-(4-(4-pyridinyl)thiophenyl)urea;

N-(5-*tert*-Butyl-3-isoxazolyl)-*N*'-(4-(4-pyridinyl)methylphenyl)urea;

N-(5-*tert*-Butyl-3-isoxazolyl)-*N*'-(4-(4-pyridinyl)thio-3-(trifluoromethyl)-

phenyl)urea;

N-(5-*tert*-Butyl-3-isoxazolyl)-*N*'-(3-(3-methyl-4-pyridinyl)thiophenyl)urea;

N-(5-*tert*-Butyl-3-isoxazolyl)-*N*'-(3-(3-methyl-4-pyridinyl)oxyphenyl)urea;

N-(5-*tert*-Butyl-3-isoxazolyl)-*N*'-(4-(3-methyl-4-pyridinyl)oxyphenyl)urea;

N-(5-*tert*-Butyl-3-isoxazolyl)-*N*'-(4-(3-methyl-4-pyridinyl)thiophenyl)urea;

N-(5-*tert*-butyl-3-isoxazolyl)-*N*'-(4-(4-(2-methylcarbamoyl)pyridyl)-

oxyphenyl) urea;

N-(5-*tert*-butyl-3-isoxazolyl)-*N*'-(3-(4-(2-methylcarbamoyl)-

pyridyl)oxyphenyl) urea;

N-(5-*tert*-butyl-3-isoxazolyl)-*N*'-(4-(4-(2-carbamoyl)pyridyl)oxyphenyl) urea;

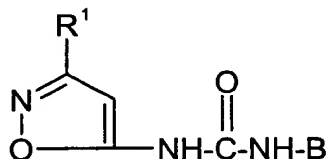
N-(5-*tert*-butyl-3-isoxazolyl)-*N*'-(3-(4-(2-carbamoyl)pyridyl)oxyphenyl) urea;

N-(5-*tert*-butyl-3-isoxazolyl)-*N*'-(3-((4-pyridyl)fluoromethyl)phenyl) urea;

N-(5-*tert*-butyl-3-isoxazolyl)-*N'*-(3-((4-pyridyl)oxomethyl)phenyl) urea;
and pharmaceutically acceptable salts thereof.

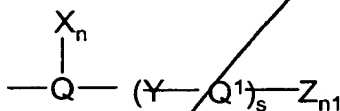
12. A method as in claim 9, wherein R¹ is t-Butyl.

13. A method as in claim 1 comprising administering a compound of the formula



wherein R¹ and B are as defined in claim 1.

14. A method as in claim 13, wherein B is 2,3-dichlorophenyl or of the formula



wherein Q is phenyl, Q¹ is phenyl, pyridinyl or benzothiazolyl, Y is -O-, -S-, -CH₂- or -NH-, Z is Cl, -CH₃ or -OCH₃, s = 0 or 1, n = 0 and n1 = 0 or 1.

15. A method as in claim 13, wherein R¹ is t-butyl.

16. A method as in claim 1 comprising administering a compound selected from the group consisting of:

N-(3-Isopropyl-5-isoxazolyl)-*N'*-(3-(4-pyridinyl)thiophenyl)urea;

N-(3-*tert*-Butyl-5-isoxazolyl)-*N'*-(2,3-dichlorophenyl)urea;

N-(3-*tert*-Butyl-5-isoxazolyl)-*N'*-(4-(4-methoxyphenyl)aminophenyl)urea;

N-(3-*tert*-Butyl-5-isoxazolyl)-*N'*-(4-(4-methoxyphenyl)oxyphenyl)urea;

N-(3-*tert*-Butyl-5-isoxazolyl)-*N'*-(4-(4-pyridinyl)oxyphenyl)urea;

N-(3-*tert*-Butyl-5-isoxazolyl)-*N'*-(4-(4-pyridinyl)thiophenyl)urea;

N-(3-*tert*-Butyl-5-isoxazolyl)-*N'*-(4-(4-pyridinyl)methylphenyl)urea;

N-(3-(1,1-Dimethylpropyl)-5-isoxazolyl)-*N'*-(4-(4-pyridinyl)methylphenyl)urea;

N-(3-(1,1-Dimethylpropyl)-5-isoxazolyl)-*N'*-(3-(4-pyridinyl)thiophenyl)urea;

N-(3-(1,1-Dimethylpropyl)-5-isoxazolyl)-*N'*-(4-(2-benzothiazolyl)-oxyphenyl)urea;

5 *N*-(3-(1-Methyl-1-ethylpropyl)-5-isoxazolyl)-*N'*-(4-(4-pyridinyl)oxyphenyl)urea;

N-(3-(1-Methyl-1-ethylpropyl)-5-isoxazolyl)-*N'*-(4-(4-pyridinyl)methylphenyl)urea;

N-(3-cyclobutyl-5-isoxazolyl)-*N'*-(4-(4-pyridyl)oxyphenyl) urea;

N-(3-*tert*-butyl-5-isoxazolyl)-*N'*-(4-(4-pyridyl)thiophenyl) urea;

10 *N*-(3-(1-methyl-1-ethylprop-1-yl)-5-isoxazolyl)-*N'*-(4-(4-pyridyl)oxyphenyl) urea;

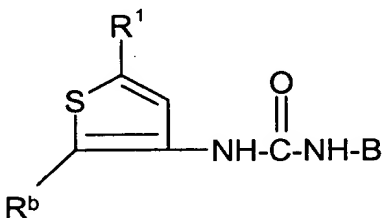
N-(3-*tert*-butyl-5-isoxazolyl)-*N'*-(4-(4-pyridyl)methylphenyl) urea;

N-(3-*tert*-butyl-5-isoxazolyl)-*N'*-(4-(4-methoxyphenyl)aminophenyl) urea;

and pharmaceutically acceptable salts thereof.

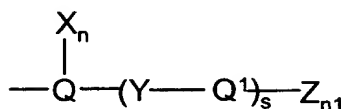
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17. A method as in claim 1 comprising administering a compound of the formula



wherein R¹, R^b and B are as defined in claim 1.

18. A method as in claim 17, wherein B is of the formula



wherein Q is phenyl, Q¹ is phenyl or pyridinyl, Y is -O- or -S- or -CH₂-, Z is OH, CH₃, Cl, -OC₂H₅ or -OC₃H₇, s = 0 or 1, n = 0 and n₁ = 0 or 1.

5

19. A method as in claim 17, wherein R¹ is t-butyl.

20. A method as in claim 17, wherein R^b is hydrogen.

10 21. A method as in claim 1 comprising administering a compound selected from the group consisting of:

N-(2-Bromo-5-*tert*-butyl-3-thienyl)-*N'*-(4-methylphenyl)urea;

N-(5-*tert*-Butyl-3-thienyl)-*N'*-(2,3-dichlorophenyl)urea;

N-(5-*tert*-Butyl-3-thienyl)-*N'*-(4-(4-hydroxyphenyl)oxyphenyl)urea;

15 *N*-(5-*tert*-Butyl-3-thienyl)-*N'*-(4-(4-ethoxyphenyl)oxyphenyl)urea;

N-(5-*tert*-Butyl-3-thienyl)-*N'*-(4-(4-isopropoxyphenyl)oxyphenyl)urea;

N-(5-*tert*-Butyl-3-thienyl)-*N'*-(4-(3-pyridinyl)oxyphenyl)urea;

N-(5-*tert*-Butyl-3-thienyl)-*N'*-(4-(4-pyridinyl)oxyphenyl)urea;

N-(5-*tert*-Butyl-3-thienyl)-*N'*-(4-(4-pyridinyl)thiophenyl)urea;

20 *N*-(5-*tert*-Butyl-3-thienyl)-*N'*-(4-(4-pyridinyl)methylphenyl)urea;

N-(5-*tert*-butyl-2-(1-thia-3,4-diazolyl))-*N'*-(4-(4-pyridyl)oxyphenyl) urea;

N-(5-*tert*-butyl-2-(1-thia-3,4-diazolyl))-*N'*-(3-(4-pyridyl)thiophenyl) urea;

N-(5-*tert*-butyl-2-(1-thia-3,4-diazolyl))-*N'*-(3-(4-methoxyphenyl)oxyphenyl)

urea;

25 *N*-(5-*tert*-butyl-2-(1-thia-3,4-diazolyl))-*N'*-(3-(4-methylphenyl)oxyphenyl)

urea;

N-(5-*tert*-butyl-3-thienyl)-*N'*-(4-(4-pyridyl)oxyphenyl) urea;

N-(5-*tert*-butyl-3-thienyl)-*N'*-(4-(4-pyridyl)thiophenyl) urea;

N-(5-*tert*-butyl-3-thienyl)-*N'*-(4-(4-pyridyl)methylphenyl) urea;

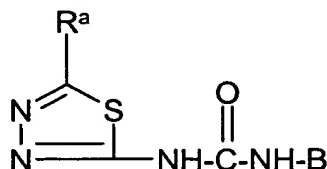
30 *N*-(5-*tert*-butyl-3-thienyl)-*N'*-(2,3-dichlorophenyl) urea;

N-(5-*tert*-butyl-3-thienyl)-*N'*-(4-(4-hydroxyphenyl)oxyphenyl) urea;

N-(5-*tert*-butyl-3-thienyl)-*N'*-(4-(4-methoxyphenyl)oxyphenyl) urea;
N-(5-*tert*-butyl-3-thienyl)-*N'*-(4-(4-ethoxyphenyl)oxyphenyl) urea;
N-(5-*tert*-butyl-3-thienyl)-*N'*-(4-(4-isopropoxyphenyl)oxyphenyl) urea;
 and pharmaceutically acceptable salts thereof.

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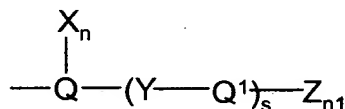
22. A method as in claim 1 comprising administering a compound of the formula



wherein R^a and B are as defined in claim 1.

10

23. A method as in claim 22, wherein B is of the formula

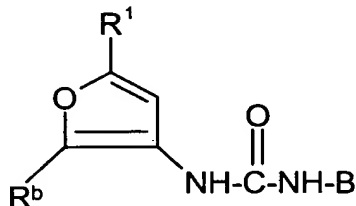


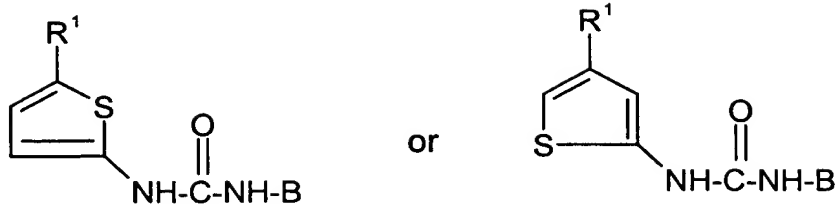
wherein Q is phenyl, Q^1 is phenyl or pyridinyl, Y is -O-, -S- or CH_2 -, Cl, $-OC_2H_5$ or $-OC_3H_7$, $s = 0$ or 1, $n = 0$ and $n1$ is 0 or 1.

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24. A method as in claim 22, wherein R^a is CF_3 - or *t*-butyl.

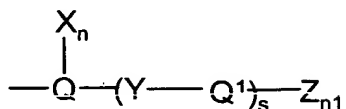
25. A method as in claim 1 comprising administering a compound of one of the formulae





wherein R^1 , R^b and B are as defined in claim 1.

26. A method as in claim 25, wherein B is of the formula



5 wherein Q is phenyl, Q^1 is phenyl or pyridinyl, Y is $-O-$, $-S-$ or $-CH_2-$, Z is OH, CH_3 , Cl, $-OC_2H_5$ or $-OC_3H_7$, $s = 0$ or 1 , $n = 0$ and $n1$ is 0 or 1 .

27. A method as in claim 25, wherein R^1 is t-butyl.

10 *Sub BS* 28. A method as in claim 1, wherein the compound for formula I displays p38 activity (IC_{50}) better than $10 \mu m$ as determined by an in-vitro kinase assay.

29. A method according to claim 1, wherein the disease is mediated by a cytokine or protease regulated by p38.

15

30. A method according to claim 1, comprising administering an amount of a compound of formula I effective to inhibit p38.

20 *Sub BS* 31. A method according to claim 1, comprising administering an amount of a compound of formula I effective to inhibit production of a disease-mediating cytokine or protease.

32. A method according to claim 1, wherein the disease is mediated by $TNF\alpha$, MMP-1, MMP-3, IL-1, IL-6 or IL-8.

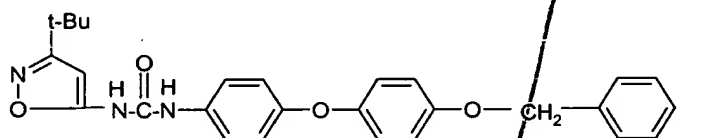
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33. A method according to claim 1, wherein the disease is an inflammatory or immunomodulatory disease.

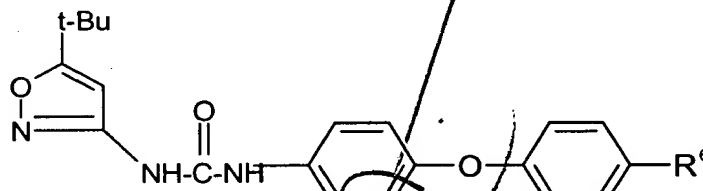
34. A method according to claim 1, wherein the disease is rheumatoid arthritis, osteoporosis, osteoarthritis, asthma, septic shock, inflammatory bowel disease, or the result of host-versus-graft reactions.

35. A compound of one of the formulae

a)

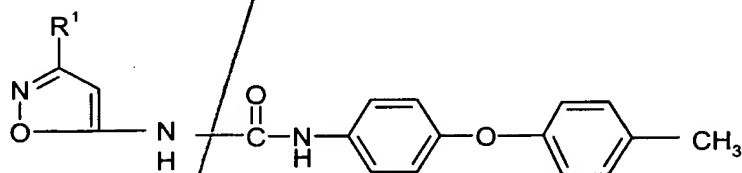


b)



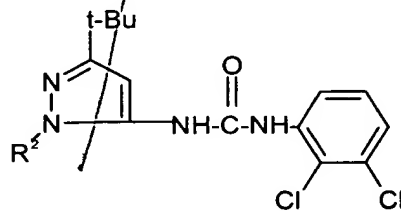
wherein R^6 is -O-CH₂-phenyl, -NH-C(O)-O-t-butyl, -O-n-pentyl, -O-n-butyl, -C(O)-N(CH₃)₂, -O-CH₂CH(CH₃)₂ or -O-n-propyl,

c)



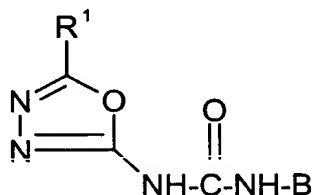
wherein R^1 is -CH₂-t-butyl;

d)



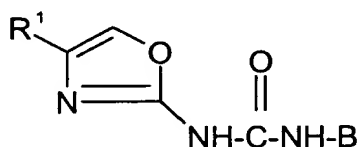
36. A pharmaceutical composition comprising a compound according to claim 35 or a pharmaceutically acceptable salt thereof and a physiologically acceptable carrier.

37. A method as in claim 1, comprising administering a compound of the formula



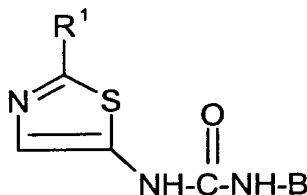
wherein R¹ and B are as defined in claim 1.

38. A method as in claim 1 comprising administering a compound of the formula



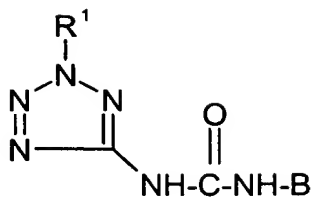
wherein R¹ and B are as defined in claim 1.

39. A method as in claim 1, comprising administering a compound of the formula



wherein R¹, R² and B are as defined in claim 1.

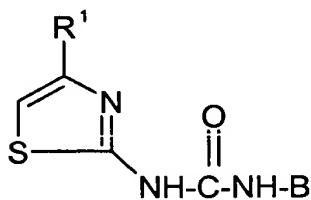
40. A method as in claim 1, comprising administering a compound of the formula



wherein R¹ and B are as defined in claim 1.

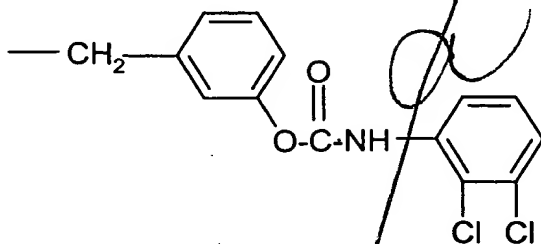
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41.

A method as in claim 1, comprising administering a compound of the formula



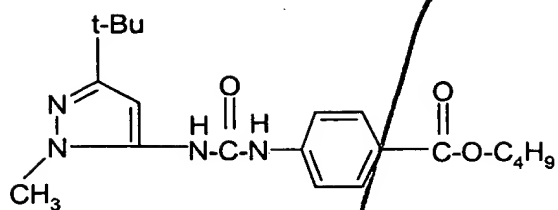
wherein R¹ and B are as defined in claim 1.

wherein R^2 is $-\text{CH}_2\text{CF}_3$, $-\text{C}_2\text{H}_4-\text{OH}$, $-\text{CH}_2-(3-\text{HOC}_6\text{H}_4)$, $-\text{CH}_2\text{C}(\text{O})\text{NHCH}_3$, $-\text{CH}_2\text{C}(\text{O})\text{OC}_2\text{H}_5$, $-\text{C}_2\text{H}_4\text{CN}$, or

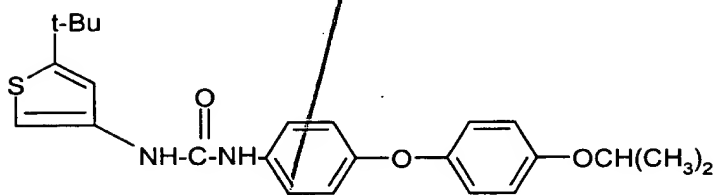


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B7

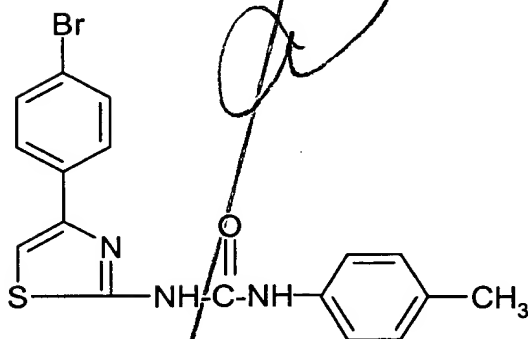
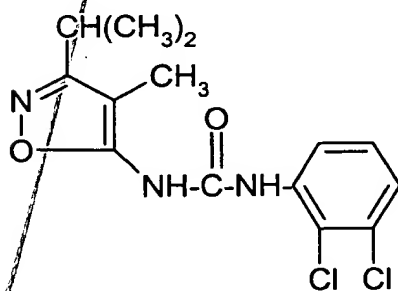
e)



5 f)



g)

10 or
h)

and pharmaceutically acceptable salts thereof.